found infected. She was hospitalized, and most of the sutures removed. A definite cellulitis, however, had set in, and multiple incisions of the leg were found necessary. The infection did not clear up, but invaded the knee joint. After several months of drainage and disability, the leg had to be amputated above the knee.

A man of twenty-two had some vague complaints referable to the abdomen and an irregular, low-grade fever. The diagnosis was obscure. A palpable node was found in the left axilla, and it was decided to remove it for biopsy. The skin was prepared with iodin and alcohol, and the tissues infiltrated with one per cent novocain. A two-centimeter incision was made over the node. However, the gland proved to be elusive and was not easily found. An excessive amount of fat called for considerable dissection and more novocain. Finally, a bit of tissue believed to be the node was removed, and the wound closed without drainage. Two days later there was redness and tenderness at the site of the incision. A cellulitis developed and repeated incisions were made. Drainage continued for many months, and the end-result was a weak, atrophic left arm with a stiff shoulder.

From the above incidents it would appear that a more critical selection of cases for local novocain anesthesia should be made, and that:

1. In the aged, on extremities, adrenalin should not be used with novocain.

2. Minor surgery under local anesthesia should be treated with the same aseptic respect as major surgery, provision being made for adequate draping, assistance, and control of bleeding.

3. Either general or regional block, rather than infiltration anesthesia, is preferable where excess fatty tissue is present, or extensive dissection is done.

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ON THE FATE OF EPINEPHRIN IN THE BODY

Pharmacologists have long known that the effects of epinephrin, injected into the animal body, are quite transient—a fact which limits its therapeutic use.[1] Just what happens to epinephrin in the animal body is not known. The hormone is readily autoxidisable *in vitro* under the conditions of pH and temperature which obtain in the body, and it has often been assumed that the same mechanism is responsible for the inactivation occurring in the body. The recent investigations of Blaschko and coworkers[2] indicate that the *in vivo* inactivation of epinephrin is indeed due to oxidation, but that such oxidation differs in important respects from the course of events *in vitro*.

As a background for consideration of the inactivation of epinephrin in the body, the facts known concerning *in vitro* oxidation will be briefly outlined. The first oxidation product appears to be an orthoquinone. On further oxidation an indole derivative is produced, which is probably responsible for the pink color appearing in epinephrin solutions on standing. Complex oxidation and polymerization follow, some eight or nine atoms of oxygen being absorbed for each molecule of epinephrin present. Sympatheticomimetic activity is probably lost with the first step in oxidation.[3]

It is unlikely that autoxidation is the sole cause of inactivation of epinephrin in the body, since various substances present in blood and other body fluids and in tissue extracts serve to delay this reaction markedly. It is now known that amino-acids, guanidine, ascorbic acid (vitamin C), cystein, glutathione, and possibly other substances serve to inhibit the autoxidation of epinephrin. The rate of disappearance of epinephrin differs in different tissues—a fact which necessitates qualification of Elliott's statement that "adrenalin disappears in the tissues which it excites."[4] For example, no disappearance of the hormone occurred on perfusing blood containing epinephrin through the hind legs or lungs. The chief site of inactivation appears to be in the liver, kidney, and small intestine. Blaschko and coworkers[2] have shown that an enzyme system is present in these tissues which brings about rapid oxidation of epinephrin. This enzyme they have named "adrenalin oxidase." In accordance with earlier work, this enzyme was shown to be absent or present in very low concentration in skeletal muscle or spleen. There is no known reason why this enzyme system should not be operative *in vivo*. It is certainly suggestive that the organs in which it has been found are those which the earlier workers discovered were chiefly responsible for the disappearance of the hormone from the circulating blood.

The oxidation of epinephrin *in vivo* differs from that *in vitro*, not only because of the presence of this enzyme system in certain tissues, and because of the widespread occurrence of inhibitors of autoxidation, particularly sulphydryl compounds, but also in the fact that the total oxygen uptake *in vitro* is seven to eight molecules of oxygen per molecule of epinephrin, whereas the total oxygen uptake *in vivo* is but four atoms per molecule. This implies a quite different chemical picture.

Summarizing: The transient effects of epinephrin in the animal body are probably attributable to oxidation of the hormone through the action of "adrenalin oxidase." This event occurs chiefly in the liver, kidney, and small intestine.

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1 Clark, A. J.: Applied Pharmacology. Fifth edition. Philadelphia. 1935.

2 Blaschko, H., Richter, D., and Schlossmann, H.: J. Physiol., 90:1, 1937.

3 Welch, A. D.: Am. J. Physiol., 108:360, 1934.

4 Elliott, T. R.: J. Physiol., 32:401, 1905.

Success, in so far as it may be gained through training, is won by cultivating such powers and attitudes of mind as interests; the habit of observing and reading; expressing one's self through conversation and discussion, through speaking and writing; intellectual curiosity and study; freedom from superstition and prejudice; open-mindedness; and the ability to profit by experience.